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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1615	

NOTIFICATION DATE	DELIVERY MODE
10/22/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/529,207	KIDOKORO ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicants' Amendments and Remarks filed 24 April 2008.

The Examiner acknowledges the following:

Claim 1 has been amended to incorporate the limitations of cancelled claim 2. Claims 3 and 4 have been amended to depend from claim 1. Claims 6 and 8-11 have been amended to eliminate improper multiple dependencies.

Claim 2 has been cancelled.

No claims have been added.

Thus, claims 1 and 3-12 are currently under consideration/pending.

WITHDRAWN OBJECTIONS/REJECTIONS

Applicants' amendment to the Title of the Invention renders the objection to the Specification moot. Thus, said objection has been withdrawn.

Applicants' amendment renders the objections under 37 CFR 1.75(c) moot. Specifically, claims 8-12 have been amended to eliminate improper multiple dependencies. Thus, said objection has been withdrawn.

Applicants' amendments render moot, the rejections to claims 1-3, 6 and 7 under 35 USC 112, second paragraph. Specifically, "substantially" has been removed from claim 1, claim 2 has been cancelled and the ratios recited in both claims 6 and 7 have been clarified. Thus, said rejections have been withdrawn.

Applicants' arguments render moot, the rejection to claim 1 under 35 USC 102(b) as being anticipated by Murakami et al. (WO 98/02185). Thus, said rejections have been withdrawn.

MAINTAINED REJECTIONS

The following rejections have been maintained from the previous Office Action dated 2 January 2008:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murakami et al. (WO 98/02185).

Murakami et al. teaches a compression-molded material, as described above. However, Murakami does not teach the specific adsorptivity values, ratios or ranges of the composition of the instant claims 2-7. Murakami does provide that "[n]o limitation is imposed on the pharmaceutical active ingredients which may be used in the present invention, and they may be added in accordance with intended uses" (col. 5, line 54-58). Table 15 of Example 13 provides an embodiment whereby the combination of the diluent (i.e. D-mannitol) and the excipient (i.e. microcrystalline cellulose) is present in a ratio of about 0.6:1 with the active ingredient (i.e. Cimetidine). Table 15 also demonstrates a 1:2.5 ratio of the diluent to the excipient within the composition. Since the amount of each ingredient of the granulated composition is adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal type and amount of active ingredient and diluent to add to the excipient composition in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these ingredient amounts would have been obvious at the time of Applicant's invention.

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejection to claims 1-7 under 35 USC 103(a) as being unpatentable over Murakami et al. have been fully considered, but they are not persuasive.

Applicant argues that the reference "neither suggests nor provides any motivation for modification to derive the particulate composition of the claimed invention".

In response, the Examiner respectfully submits that the invention to Murakami does in fact provide the teachings and suggestion to motivate the skilled artisan to prepare the claimed invention. Method 3 (col. 8, lines 15-24) expressly teaches combining an excipient, erythritol, an active ingredient, as necessary, and an additive, and forming a composition, which is dried to intermediately form granules. The resulting mixture is substantially dried and compression-molded (i.e. formed into a tablet). Murakami further expressly teaches the instantly claimed pantethine as a type of vitamin active ingredient (col. 5, lines 61-67 and claims 12 and 13). Light anhydrous silicic acid is expressly taught as a diluent or additive (col. 7, lines 13-25) and microcrystalline cellulose is expressly taught as an excipient of the instantly claimed composition (claims 8 and 10). The units of "weight parts" as recited in claims 4 and 5 are not clearly defined in Applicants' specification. Absent said definition, the Examiner broadly and reasonably interprets the relative proportions of the combined silicic acid and microcrystalline cellulose to pantethine as a ratio of the combined additives to the active ingredient. Similarly, claims 6 and 7 recite limitations to the ratio of silicic acid to microcrystalline cellulose within the composition (i.e. additive/excipient ratios). Though the claimed proportions and ratios are not expressly taught, adjustment of instantly claimed components such as the excipient and the active ingredient is certainly suggested. Claims 5-7 teach the excipient in combination with erythritol as being present in a range as wide as 5-99% by weight of the composition to as narrow as 20-50% by weight. Similarly, the active ingredient is expressly taught as being present in amounts ranging as wide as 1-70% by weight of the composition to as narrow as 1-30% by weight. So in view of the aforementioned methods, and though not expressly taught,

adjustment of the proportions and ratios as instantly recited in claims 4-7, would have been well within the realm of routine experimentation for an artisan of ordinary skill.

Thus, for these reasons, Applicants' arguments are found unpersuasive. Said rejection is maintained.

NEW REJECTIONS

In light of Applicants' amendments, the following rejections have been newly added:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The currently amended claim 1 contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. As amended, the instant claim 1 recites two additional limitations: (1) "wherein an adsorptivity is 0.6 or higher" and (2) "wherein … adsorptivity is a ratio of a total of a weight of the light anhydrous silicic acid and *a light anhydrous silicic acid weight equivalency*, relative to pantethine absorption, of the microcrystalline cellulose, to a weight of the pantethine" [emphasis added]. The Examiner acknowledges the first added limitation as having support in the originally submitted claim 2, which is presently cancelled. However, Applicants' response,

dated 24 April 2008, neither specifically discusses nor supports the addition of the second limitation to the rejected claim 1. Having carefully examined the instant disclosure, notably pages 4-5 and Tables 2-4, the Examiner respectfully submits that support for the amended claim 1is lacking and the addition of said limitations constitutes **new matter**. The Examiner further searched the specification and respectfully submits that while general support for the "adsorptivity" limitation is found, support for limitations such as a "light anhydrous silicic acid weight equivalency" or said "equivalency relative to other properties of the composition (i.e. pantethine absorption) was not found. Furthermore, the specification is silent to the general concept of *ad*sorptivity being defined as a ratio of components relative to "pantethine *ab*sorption" [emphasis added], making it further unclear to the Examiner how adsorptivity is a function of absorption. Broadly and reasonably interpreted, the new limitations have been considered and are deemed by the Examiner to be properties of the instantly claimed composition. With regard to said limitations as recited in the amended claim 1, until some material difference in the properties of the compositions are demonstrated, said limitations are considered by the Examiner to be directed toward the instantly claimed composition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murakami et al. (WO 98/02185).

The instant claims 1 and 3 are directed to a particulate comprising pantethine, light anhydrous silicic acid and microcrystalline cellulose, as discussed above. The limitation recited in claim 3 wherein the adsorptivity range of the composition is further limited to 0.6-0.7, is also considered by the Examiner as a property of the composition for the reasons discussed above. Ratios and proportions of the components to one another are recited (claims 4-7). Percentages of pantethine by weight of the composition are recited (claims 8 and 9). A range for the average particle size of the composition is recited (claim 10). Independent claim 11 recites a solid dosage form comprising the particulate composition of claim 1. Claim 12 further limits said form to one such as powders, granules or tablets.

The teachings to Murakami et al. regarding claims 1 and 3-7 are discussed above. Murakami further expressly teaches that the presence of the active ingredient in the composition is at least 50% by weight and/or present in a range from 50-60% by weight (col. 7, lines 6-9). The methods preparation (col. 8, lines 6-24) teach the formation of granules. Claim 16 teaches a formation of the composition into a solid dosage form such as a tablet.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising pantethine, light anhydrous silicic acid and microcrystalline cellulose, as suggested by Murakami, modify the levels or proportions of the ingredients, and produce the instant solid dosage form invention.

One of ordinary skill in the art would have been motivated to do this because Murakami expressly teaches methods for producing solid dose forms (e.g. granules) using the general components which are instantly claimed, notably an excipient, an additive and an active ingredient, which are further expressly taught, as discussed above. One with ordinary skill in the art would vary the levels of these materials as well as the granule size, within the ranges taught by Murakami, during the process of routine experimentation in order to optimize properties such as the release profile of the pantethine.

The reference does not expressly teach the average particle size range, as claimed by Applicants. Since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. For example, Examples 1 and 5 expressly teach sieving of prepared granules using a #16 mesh screen, ensuring granule size of 1,000 microns or smaller. Thus, it would have been customary for an artisan of ordinary skill, to employ a range of different sized mesh screens, such as from a #60 mesh to a #120 mesh or a metric range of 125-250 microns (see Particle size-Sieve mesh conversion chart at www.sigmaaldrich.com), as a way to optimally size the granules compressed within the composition. Thus, absent some demonstration of unexpected results from the

claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

All claims have been rejected; no claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615